

## REMARKS

### Status of the Claims

Claims 1, 19, and 30 are amended herein and claim 5 is cancelled. After entering the current amendments, claims 1-4 and 6-45 are pending and under examination.

Claims 1 and 30 are amended to more clearly define the scope of Applicant's claimed invention. Claim 19 is amended to correct a typographical error. No new matter is added by these amendments. All cancellations are made without prejudice and Applicant reserves the right to prosecute cancelled subject matter in related patent applications.

### Rejections under 35 U.S.C. §112, second paragraph

Claims 1-45 stand rejected for indefiniteness. The Examiner alleges that it is unclear what is meant by "said oxygen-18 labeled organic acid is not oxygen-18 labeled homovanillic acid or includes at least two oxygen-18 labeled organic acids." As an initial matter, Applicant points out that this rejection applies only to claims 1-8 and 30-36. The remaining claims do not encompass the allegedly indefinite claim term. Applicant respectfully disagrees with the Examiner's allegation of indefiniteness; however, this rejection is rendered moot by the instant claim amendments. Accordingly, this rejection is traversed and should be withdrawn.

### Rejection under 35 U.S.C. §103(a)

Claims 1-45 stand rejected as obvious over Magera et al. (Clinica Chimica Acta, 306: 35-41, 2000; "Magera") in view of Youhnovski et al. (Z. Naturforsch, 58c: 268-279, 2003; "Youhnovski"). This rejection is traversed by the instant claim amendments and the rejection as it applies to each pending independent claim is addressed individually below.

Magera teaches a method for quantifying unlabeled homovanillic acid in urine using either GC-MS or LC-MS. The Magera method adds oxygen-18 labeled homovanillic acid to the sample as an internal standard. The amount of labeled and unlabeled homovanillic acid is

measured and the amount of labeled homovanillic acid is used to adjust for the amount of unlabeled homovanillic acid loss during processing in order to relate the amount of detected homovanillic acid to the amount present in the original sample.

Youhnovski teaches a method for quantifying the amount of 9-HODEs<sup>1</sup> and 13-HODEs<sup>2</sup> in a blood sample. The Youhnovski method adds a standard solution containing oxygen-18 labeled 9-HODE and 13-HODE to the blood samples. The amount of labeled and unlabeled acids are measured and the labeled acids are used to adjust for analyte loss during processing in order to relate the amount of detected 9-HODE and 13-HODE to the amount present in the original sample.

The methods of Magera and Youhnovski are similar in several respects. Both prior art references are concerned with the detection of organic acids from the class of hydroxy mono-acids. Furthermore, each prior art method uses an oxygen-18 labeled internal standard containing only those organic acids that will be detected and quantified. Thus, the prior art does not teach or suggest using an internal standard containing an oxygen-18 labeled organic acid other than a hydroxy mono-acid. Specifically, there is no suggestion to use an oxygen-18 labeled dihydroxy mono-acid, dicarboxyl organic acid, hydroxyl dicarboxyl acid, tricarboxyl acid, glycine conjugate, or oxo acid.

#### Claims 1-4, 6-8, and 30-36

Claims 1-4, 6-8, and 30-36 encompass methods for measuring the amounts of unlabeled organic acids using a standard (e.g., an internal standard) that must contain at least one oxygen-18 labeled organic acid other than a hydroxy mono-acid. As discussed above, this limitation is clearly absent from the cited prior art. Specifically, the cited prior art does not suggest the use of an oxygen-18 labeled dihydroxy mono-acid, dicarboxyl organic acid, hydroxyl dicarboxyl acid, tricarboxyl acid, glycine conjugate, or oxo acid.

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<sup>1</sup> 9-HODE refers to 9-hydroxy-10,12-octadecadienoic acid.

<sup>2</sup> 13-HODE refers to 13-hydroxy-9,11-octadecadienoic acid.

Magera uses an internal standard containing only oxygen-18 labeled homovanillic acid; a hydroxy mono-acid. There is no suggestion or motivation to add a labeled acid belong to an entirely different class of acids, because Magera was only interested in measuring a single compound.

Youhnovski uses an internal standard containing two oxygen-18 labeled organic acids. However, each of these acids also belongs to the hydroxy mono-acid class of organic acids. There is no suggestion or motivation to add additional labeled acids from classes other than the hydroxy mono-acid class, to the internal standard because Youhnovski was interested in measuring only hydroxyoctadecadienoic acids, a very narrow subset of hydroxy monoacids.

Accordingly, the cited prior art does not teach or suggest every element of claims 1-4, 6-8, and 30-36 because there is no suggestion to use an internal standard containing oxygen-18 labeled dihydroxy mono-acid, dicarboxyl organic acid, hydroxyl dicarboxyl acid, tricarboxyl acid, glycine conjugate, or oxo acid. The prior art provides no motivation to include additional oxygen-18 labeled organic acids from other acid classes in the internal standard because each reference is concerned with detecting only a single compound, or a very narrow subset of a single acid class. Thus, the cited prior art fails to establish a *prima facie* case of obviousness. This rejection is traversed and should be withdrawn.

#### Claims 9-29 and 37-45

Claims 9-29 and 37-45 encompass methods and compositions that require the combination of at least seven different oxygen-18 labeled organic acids. Claims 9 and 37, for example, require at least one labeled organic acid selected from each of the acid classes of hydroxy mono-acid, dihydroxy mono-acid, dicarboxyl organic acid, hydroxyl dicarboxyl acid, tricarboxyl acid, glycine conjugate and oxo acid, is added to the sample.

As discussed above, the prior art cited by the Examiner is concerned with the detection of organic acids belonging to only a single acid class. In view of the limited nature of the prior art detection methods, there is no suggestion or motivation to make or use a standard solution containing at least seven different labeled organic acids, representing seven different organic acid

classes. Applicant respectfully submits that the rejection of claims 9-29 and 37-45 is traversed and should be withdrawn.

### CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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